Possibility of a New Anti-Alzheimer's Disease Pharmaceutical Composition Combining Memantine and Vitamin D

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Résumé en anglais	Alzheimer's disease (AD) is the leading cause of dementia. In addition to a decrease in brain cholinergic activity, AD is also marked by glutamatergic excitotoxicity that results in neuronal death, characterized clinically by a loss of learning and memory abilities. The currently available drugs for symptomatic treatment of AD (i.e. memantine and acetylcholinesterase inhibitors) only temporarily slow down the natural history of the disease process. Among them, memantine is the only one that acts as a non-competitive low-affinity modulator of N-methyl-D-aspartate (NMDA) receptors. Memantine's modulation of NMDA receptors has been reported to prevent the neuronal necrosis induced by glutamatergic calcium neurotoxicity, but not the neuronal apoptosis resulting from oxidative stress. This observation calls for new drug regimen strategies based on memantine combined with molecules having antioxidant effects, in order to create a multi-target therapy to increase neuronal protection and prevent AD progression. We wish to highlight that vitamin D is a secosteroid hormone that is suggested to have neuroprotective effects that include regulation of neuronal calcium homeostasis, as well as antioxidant, neurotrophic and anti-inflammatory properties. The combination of memantine plus vitamin D may provide, in one treatment, enhanced protection against several degenerative processes linked to AD. Based on the present rationale, a clinical trial testing this hypothesis is currently in recruitment (AD-IDEA trial; ClinicalTrials.gov identifier: NCT01409694). This new pharmaceutical composition may provide an effective solution to the problem of neuronal death and cognitive decline in AD.
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Titre abrégé	Drug Aging

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